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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,793	04/24/2006	Irina A Buhimschi	035394-0286	4143
54077 7590 12/11/2008 CIPHERGEN c/o FOLEY & LARDNER LLP 3000 K STREET NW SUITE 500 WASHINGTON, DC 20007				
EXAMINER				
COOK, LISA V				
ART UNIT		PAPER NUMBER		
1641				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/541,793

**Applicant(s)**

BUHIMSCHI ET AL.

**Examiner**

LISA V. COOK

**Art Unit**

1641

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 13 August 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-55 is/are pending in the application.
- 4a) Of the above claim(s) 1-20, 24-28, 33, 34 and 38-55 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21-23, 29-32 and 35-37 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
- Paper No(s)/Mail Date 7/11/05 & 5/10/07
- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## DETAILED ACTION

### ***Restriction Election***

1. Applicant's election without traverse of Group II (claims 21-37) in the reply filed on 8/13/08 is acknowledged. Applicant has also elected the species of claim 23-ELISA and claim 32-tocolytic for consideration with out traverse (response filed 8/13/08).
2. Claims 1-20, 24-28, 33, 34, and 38-55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/13/08.
3. Currently claims 21-23, 29-32, and 35-37 are under consideration.

### ***Priority***

4. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number. This application does not contain the required first sentence of the specification referencing application no. PCT/US2003/036118 filed 11/13/03 and application no. 60/444,976 filed 2/4/03. Please add to the specification.

***Information Disclosure Statement***

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on PTO-1449 has cited the references they have not been considered.
6. The information disclosure statement filed 5/10/07 has been considered as to the merits before First Action.
7. The information disclosure statement filed 7/11/05 has been considered as to the merits before First Action.

***Specification***

8. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

***Claim Objections***

9. Claim 23 is objected to because of the following informalities: Claim 23 utilizes the acronym ELISA. Although the terms may have art-recognized meanings, it is not clear if applicant intends to claim any prior art definition of the abbreviations. In the specification on page 30 section 0086, for example, ELISA is defined as enzyme-linked immunoassay. This definition should be added to claim 23. The term should be defined in its first instance. The initial explanation will convey intended meaning of subsequent abbreviations in the claims. Please define.

### ***Specification***

10. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

11. The use of several trademarks is noted in this application. They should be capitalized wherever they appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks. (For example, see pages 18 and 21 – EPOXIDE, etc).

### ***Claim Rejections - 35 USC § 102***

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 21, 22, 23, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Cederberg et al. (Diabetologia, 2001, Vol.44, pages 766-774).

Cederberg et al. disclose ELISA procedures to measure protein carbonyls (i.e. carbonylated peptides) in plasma (claims 21 and 23). Although Cederberg et al. are silent with respect to the plasma sample being vaginal, it is noted that this is deemed inherent because regardless of the sampling source plasma is still plasma. The samples were incubated with 2,4-dinitrophenylhydrazine solution (claims 22 and 37) and measured at 490nm in a spectrophotometer. See abstract and page 768, 1<sup>st</sup> column 5<sup>th</sup> paragraph. The researchers found that diabetic pregnancy (diagnostic or prognostic determination) yielded increase rates of lipid peroxidation and protein carbonylation in the mother and in the fetus. See page 771, 2<sup>nd</sup> column – Discussion.

***Claim Rejections - 35 USC § 103***

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

II. Claims 29, 30 and 31 are rejected under 35 U.S.C. 103(a) as being obvious over Cederberg et al. (Diabetologia, 2001, Vol.44, pages 766-774) in view of Cederberg et al. (Pediatric Research, Vol. 49, No.6, 2001, pages 755-762).

Please see Cederberg et al. (Diabetologia, 2001, Vol.44, pages 766-774) as set forth above.

Cederberg et al. (Diabetologia, 2001, Vol.44, pages 766-774) differ from the instant invention in not specifically teaching treatment and/or treatment recommendations in diabetic pregnancies via carbonyl peptide measurements.

However, Cederberg et al. (Pediatric Research, Vol. 49, No.6, 2001, pages 755-762) teach methods evaluating fetal livers for protein carbonylation. See page 757, 1<sup>st</sup> column, 3<sup>rd</sup> paragraph. The study monitored dietary supplementation of a combination of two antioxidants (vitamin E and vitamin C) in diabetic rat pregnancy (Applicant's treatment).

The combined antioxidant treatment with vitamin E and vitamin C decreased fetal malformation rate and diminished oxygen radical –related tissue damage. See abstract.

The measurement of protein carbonylation exemplified a gradual reduction of the diabetes-induced protein damage in fetal livers with increasing-dosage of the administered antioxidants. See page 759, last paragraph.

It would have been obvious to one of ordinary skill in the art at the time of applicant's invention to monitor treatments as taught by Cederberg et al. (Pediatric Research, Vol. 49, No.6, 2001, pages 755-762) in the protein carbonylation procedure of Cederberg et al. (Diabetologia, 2001, Vol.44, pages 766-774) because Cederberg et al. (Pediatric Research, Vol. 49, No.6, 2001, pages 755-762) taught that the measurement of protein carbonylation exemplified a gradual reduction of the diabetes-induced protein damage in fetal livers with increasing-dosage of the administered antioxidants. See page 759, last paragraph. ). The combined antioxidant treatment of vitamin E and vitamin C decreased fetal malformation rate and diminished oxygen radical –related tissue damage. See abstract.

III. Claim 32 is rejected under 35 U.S.C. 103(a) as being obvious over Cederberg et al. (Diabetologia, 2001, Vol.44, pages 766-774) in view of Cederberg et al. (Pediatric Research, Vol. 49, No.6, 2001, pages 755-762) and further in view of Mitzkat et al. (Zeitschrift fur Geburtshilfe und Perinatologie, 1978, Vol.182, No.5, pages 331-342, English Abstract).



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Please see Cederberg et al. (Diabetologia, 2001, Vol.44, pages 766-774) in view of Cederberg et al. (Pediatric Research, Vol. 49, No.6, 2001, pages 755-762) as set forth above.

Cederberg et al. (Diabetologia, 2001, Vol.44, pages 766-774) in view of Cederberg et al. (Pediatric Research, Vol. 49, No.6, 2001, pages 755-762) differ from the instant invention in not specifically teaching tocolytic treatment.

However, Mitzkat et al. teach procedures for evaluating diabetic pregnancies via tocolytic treatments in hyperglycemic and/or hypoglycemic reactions. Monitoring tocolytic treatments could aid in their mode of action and their effects on diabetic pregnancies. See English abstract.

It would have been obvious to one of ordinary skill in the art at the time of applicant's invention to monitor tocolytic treatments as taught by Cederberg et al. (Pediatric Research, Vol. 49, No.6, 2001, pages 755-762) in view of Cederberg et al. (Diabetologia, 2001, Vol.44, pages 766-774) because Mitzkat et al. taught that monitoring tocolytic treatments could aid in their mode of action and their effects on diabetic pregnancies. See English abstract.

**IV.** Claims 35 and 36 are rejected under 35 U.S.C. 103(a) as being obvious over Cederberg et al. (Diabetologia, 2001, Vol.44, pages 766-774) in view of Yates et al. (U.S. Patent #5,538,897).

Please see Cederberg et al. (Diabetologia, 2001, Vol.44, pages 766-774) as set forth above.

Cederberg et al. (Diabetologia, 2001, Vol.44, pages 766-774) differ from the instant invention in not specifically teaching mass spectrometric analysis of the peptide fragments (carbonyl peptide) measurements.

However, Yates et al. disclose a method of correlating a peptide fragment with amino acid sequences derived from a database. A peptide is analyzed by a tandem mass spectrometer to yield a peptide fragment mass spectrum (mass fingerprinting). A protein sequence database or a nucleotide sequence database is used to predict/identify the fragment. For each candidate sequence, a plurality (pool) of fragments of the sequences is identified and the masses-m/z ratios of the fragments are predicted and used to form a predicted mass spectrum. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize tandem mass spectrometry database sequence comparison as taught by Yates et al. to identify the fragments found in the method of in the protein carbonylation procedure of Cederberg et al. (Diabetologia, 2001, Vol.44, pages 766-774), because Yates et al. taught that the patented system for correlating fragment spectra with known sequences would avoid delay and/or subjectivity in hypothesizing or deducing candidate amino acid sequences from the fragment spectra. (Column 1 lines 44-62).

One having ordinary skill in the art would have been motivated to do this because in order to achieve maximal data processing/protein manipulation to determine the parameter of interest.

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14. For reasons aforementioned, no claims are allowed.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, can be reached on (571) 272-0806.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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12/5/08*

/Lisa V. Cook/  
Primary Examiner, Art Unit 1641